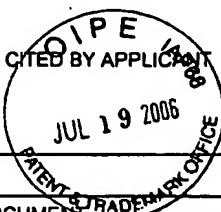
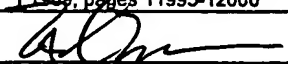
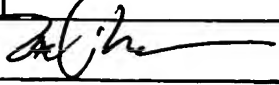
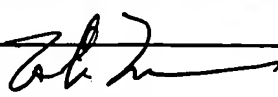
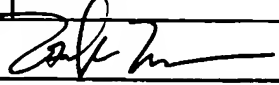



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| LIST OF REFERENCES CITED BY APPLICANT<br><br>   |    |  |           | APPLICANT<br>Michael R JOHNSON   |                                 |  |                               |
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| U.S. PATENT DOCUMENTS  |    |  |           |                                  |                                 |  |                               |
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| ZT   | AO | WO 00/23023  | 4/27/2000 | WIPO                             |                                 |  |                               |
| ZT   | AP | WO 01/05773 A1   | 1/25/2001 | WIPO                             |                                 |  |                               |
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| OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)  |    |  |           |                                  |                                 |  |                               |
| ZT   | AV | Maria E. GIANNAKOU, et al., "Characterization of the <i>Drosophila melanogaster</i> alkali-metal/proton exchanger (NHE) gene family", The Journal of Experimental Biology, XP-002381331, vol. 204, no. 21, 2001, pages 3703-3716   |           |                                  |                                 |  |                               |
| ZT   | AW | Pascal BARBRY, et al., "Biochemical Identification of Two Types of Phenamil Binding Sites Associated with Amiloride-Sensitive Na <sup>+</sup> Channels", Biochemistry, XP-002381332, vol. 28, no. 9, 1989, pages 3744-3749   |           |                                  |                                 |  |                               |
| ZT   | AX | Pascal BARBRY, et al., "[ <sup>3</sup> H]Phenamil Binding Protein of the Renal Epithelium Na <sup>+</sup> Channel. Purification, Affinity Labeling, and Functional Reconstitution", Biochemistry, XP-002381333, vol. 29, no. 4, 1990, pages 1039-1045                                      |           |                                  |                                 |  |                               |
| ZT   | AY | Jeanne VELLY, et al., "Effects of amiloride and its analogues on [ <sup>3</sup> H]batrachotoxinin-A 20- $\sigma$ benzoate binding. [ <sup>3</sup> H]tetracaine binding and <sup>22</sup> Na influx", European Journal of Pharmacology, XP-002381334, vol. 149, no. 1-2, 1988, pages 97-105 |           |                                  |                                 |  |                               |
| ZT   | AZ | Thomas R. KLEYMAN, et al., "The Cellular Pool of Na <sup>+</sup> Channels in the Amphibian Cell Line A6 Is Not Altered by Mineralocorticoids", THE JOURNAL OF BIOLOGICAL CHEMISTRY, XP-002381335, vol. 264, no. 20, July 15, 1989, pages 11995-12000                                       |           |                                  |                                 | <input type="checkbox"/> Additional References sheet(s) attached |                               |
| Examiner<br>  |    |  |           |                                  | Date Considered 19 OCTOBER 2006 |  |                               |
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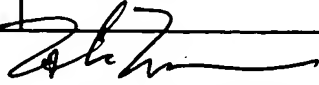
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| ZT   | AA   | 4,177,285  | 12-04-79  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AB   | 3,794,734  | 02-26-74  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AC   | 3,864,401  | 02-04-75  | Schultz et al.                         | ---          |                               |
| ZT   | AD   | 3,914,253  | 10-21-75  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AE   | 3,929,872  | 12-30-75  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AF   | 3,931,239  | 01-06-76  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AG   | 3,953,476  | 04-27-76  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AH   | 3,966,966  | 06-29-76  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AI   | 4,006,180  | 02-01-77  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AJ   | 4,012,524  | 03-15-77  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AK   | 4,159,279  | 06-26-79  | Smith et al.                           | ---          |                               |
| ZT   | AL   | 4,163,781  | 08-07-79  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AM   | 4,163,794  | 08-07-79  | Cragoe, Jr. et al.                     | ---          |                               |
| ZT   | AN   | 4,085,219  | 04-18-78  | Cragoe, Jr. et al.                     | ---          |                               |
| <b>FOREIGN PATENT DOCUMENTS</b>  |  |  |   |  |              |                               |
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| <b>OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)</b>   |  |  |   |  |              |                               |
| ZT   | AW   | R. Tarran et al., <u>The CF Salt Controversy: In Vivo Observations and Therapeutic Approaches</u> , <i>Molecular Cell</i> , Vol. 8, 149-158, July 2001.                                |   |  |              |                               |
| ZT   | AX   | Michael R. Knowles et al., <u>Amiloride in Cystic Fibrosis: Safety, Pharmacokinetics, and Efficacy in the Treatment of Pulmonary Disease</u> , Chapter 20, page 301-316. <u>1992</u>   |   |  |              |                               |
| ZT   | AY   | Louis Simchowicz et al., <u>An Overview of the Structure Activity Relations in the Amiloride Series</u> , Chapter 2, page 9-25. <u>1992</u>  |   |  |              |                               |
| ZT   | AZ   | J.R. Sabater et al., <u>Aerosolization of P2y2-Receptor Agonists Enhances Mucociliary Clearance in Sheep</u> , <i>The American Physiological Society</i> , page 2191-2198. <u>1999</u> |   |  |              |                               |
| Examiner    |  |  |   | Date Considered <u>19 OCTOBER 2006</u> |              |                               |
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| U.S. PATENT DOCUMENTS  |    |  |          |  |  |   |                               |
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| <u>ET</u>  | AA | 4,025,625  | 05-24-77 | Rooney et al.                                |  |   |                               |
| <u>ET</u>  | AB | 4,196,292  | 04-01-80 | Woltersdorf, Jr. et al.                      |  |   |                               |
| <u>ET</u>  | AC | 4,087,526  | 05-02-78 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AD | 4,087,542  | 05-02-78 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AE | 4,092,414  | 05-30-78 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AF | 4,100,294  | 07-11-78 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AG | 4,105,769  | 08-08-78 | Rooney et al.                                |  |   |                               |
| <u>ET</u>  | AH | 4,140,776  | 02-20-79 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AI | 4,145,551  | 03-20-79 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AJ | 4,181,727  | 01-01-80 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AK | 4,237,130  | 12-02-80 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AL | 4,237,144  | 12-02-80 | Cragoe, Jr. et al.                           |  |   |                               |
| <u>ET</u>  | AM | 4,277,602  | 07-07-81 | Woltersdorf et al.                           |  |   |                               |
| <u>ET</u>  | AN | 4,291,050  | 09-22-81 | Woltersdorf, Jr. et al.                      |  |   |                               |
| FOREIGN PATENT DOCUMENTS   |    |  |          |  |  |   |                               |
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| OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)  |    |  |          |  |  |   |                               |
| <u>ET</u>  | AW | Thomas R. Kleyman et al., <u>Amiloride and Its Analogs as Tools in the Study of Ion Transport</u> , <i>The Journal of Membrane Biology</i> , Vol. 105, pages 1-21, 1988. |          |  |  |   |                               |
| <u>ET</u>  | AX | Edward C. Taylor et al., <u>A Facile Route to "Open Chain" Analogues of DDATHE</u> , <i>Heterocycles</i> , Vol. 28, No. 2, 1989.   |          |  |  |   |                               |
| <u>ET</u>  | AY | Paul-Michael Windscheif et al., <u>Substituted Dipyridlethenes and -ethynes and Key Pyridine Building Blocks</u> , <i>Synthesis</i> , pages 87-92, January 1994.         |          |  |  |   |                               |
| <u>ET</u>  | AZ | Edward J. Cragoe, Jr., <u>The Synthesis of Amiloride and Its Analogs</u> , page 24-38, Chapter 3. <u>1992</u>  |          |  |  |   |                               |
| Examiner    |    |  |          |  | Date Considered <u>19 OCTOBER 2006</u> |   |                               |
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| <u>ET</u>  | AA | 4,003,927  | 01-18-77 | Woltersdorf, Jr. et al.                                 |  |  |                               |
| <u>ET</u>  | AB | 4,296,122  | 10-20-81 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AC | 4,317,822  | 03-02-82 | Woltersdorf, Jr. et al.                                 |  |  |                               |
| <u>ET</u>  | AD | 4,362,724  | 12-07-82 | Bock et al.   |  |  |                               |
| <u>ET</u>  | AE | 4,401,669  | 08-30-83 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AF | 3,974,212  | 08-10-76 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AG | 3,984,465  | 10-05-76 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AH | 3,984,552  | 10-05-76 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AI | 4,067,980  | 01-10-78 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AJ | 4,085,117  | 04-18-78 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AK | 4,085,211  | 04-18-78 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AL | 4,246,406  | 01-20-81 | Cragoe, Jr. et al.                                      |  |  |                               |
| <u>ET</u>  | AM | 3,472,848  | 10-14-69 | Edward J. Cragoe, Jr. et al.                            |  |  |                               |
| <u>ET</u>  | AN | 3,544,571  | 12-01-70 | Edward J. Cragoe, Jr., et al.                           |  |  |                               |
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| <b>OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)</b>   |    |  |          |   |  |  |                               |
| <u>ET</u>  | AW | Jack H. Li, et al., <u>Stereoselective Blockage of Amphibian Epithelial Sodium Channels by Amiloride Analogs</u> , <i>The Journal of Pharmacology and Experimental Therapeutics</i> , Vol. 267, No. 3, pages 1081-1084, 1993.                    |          |   |  |  |                               |
| <u>ET</u>  | AX | Pallav L. Shah, M.D., <u>Chapter 7. Progress in the Treatment of Pulmonary Disease in Cystic Fibrosis</u> , <i>Annual Reports in Medicinal Chemistry</i> , Vol. 36, pages 67-76, 2001.   |          |   |  |  |                               |
| <u>ET</u>  | AY | Dieter Worlitzsch et al., <u>Effects of Reduced Mucus Oxygen Concentration in Airway Pseudomonas Infections of Cystic Fibrosis Patients</u> , <i>The Journal of Clinical Investigation</i> , February 2002, Volume 109, Number 3, pages 317-336. |          |   |  |  |                               |
| <u>ET</u>  | AZ | Edward J. Cragoe, Jr., et al., <u>Chapter 7: Diuretic Agents</u> , <i>Annual Reports in Medicinal Chemistry</i> , 1966, page 59-68.  |          |   |  |  |                               |
| Examiner <u>ET</u>   |    |  |          |   | Date Considered <u>19 OCTOBER 2006</u> |  |                               |
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| <u>ET</u>  | AA   | 3,991,106   | 11-09-76   | Cragoe, Jr., et al.   | —                                      | —            |                               |
| <u>ET</u>  | AB   | 3,991,087   | 11-09-76   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AC   | 3,989,749   | 11-02-76   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AD   | 3,987,091   | 10-19-76   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AE   | 3,979,361   | 09-07-76   | Schultz et al.        | —                                      | —            |                               |
| <u>ET</u>  | AF   | 3,976,686   | 08-24-76   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AG   | 3,976,681   | 08-24-76   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AH   | 3,958,004   | 05-18-76   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AI   | 3,956,374   | 05-11-76   | Shepard et al.        | —                                      | —            |                               |
| <u>ET</u>  | AJ   | 3,928,624   | 12-23-75   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AK   | 3,894,065   | 07-08-75   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AL   | 3,668,241   | 06-06-72   | Cragoe, Jr. et al.    | —                                      | —            |                               |
| <u>ET</u>  | AM   | 3,625,950   | 12-07-71   | Edward J. Cragoe, Jr. | —                                      | —            |                               |
| <u>ET</u>  | AN   | 4,298,743   | 11-03-81   | Cragoe, Jr. et al.    | —                                      | —            |                               |
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| <b>OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)</b>   |  |   |  |                       |  |              |                               |
| <u>ET</u>  | AW   | Edward J. Cragoe, Jr., et al., <u>Chapter 7: Diuretic Agents</u> , <i>Annual Reports in Medicinal Chemistry</i> , 1965, page 67-77.                             |  |                       |  |              |                               |
| <u>ET</u>  | AX   | Robert L. Smith, et al., <u>Chapter 8: Diuretics</u> , <i>Annual Reports in Medicinal Chemistry</i> , Volume 11, pages 71-79, 1976.                             |  |                       |  |              |                               |
| <u>ET</u>  | AY   | Robert L. Smith, et al., <u>Chapter 7: Diuretics</u> , <i>Annual Reports in Medicinal Chemistry</i> , Volume 13, pages 61-70, 1978.                             |  |                       |  |              |                               |
| <u>ET</u>  | AZ   | Edward J. Cragoe, Jr., <u>Structure-Activity Relationships in the Amiloride Series</u> , <i>Merck Sharp and Dohme Research Laboratories</i> , 1979, pages 1-20. |  |                       |  |              |                               |
| Examiner <u></u>  |  |   |  |                       | Date Considered <u>19 OCTOBER 2006</u> |              |                               |
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| LIST OF REFERENCES CITED BY APPLICANT  |    |  |          | APPLICANT                                      |  |  |                               |
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| <b>U.S. PATENT DOCUMENTS</b>   |    |  |          |  |  |  |                               |
| EXAMINER<br>INITIAL  |    | DOCUMENT<br>NUMBER   | DATE     | NAME   | CLASS                                  | SUB<br>CLASS   | FILING DATE<br>IF APPROPRIATE |
| <u>BT</u>  | AA | 3,313,813  | 04/11/67 | Cragoe   |  |  |                               |
| <u>BT</u>  | AB | 3,573,306  | 03/30/71 | K.L. Shepared et al.                           |  |  |                               |
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| <b>FOREIGN PATENT DOCUMENTS</b>  |    |  |          |  |  |  |                               |
|  |    | DOCUMENT<br>NUMBER   | DATE     | COUNTRY  | TRANSLATION<br>YES NO                  |  |                               |
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| <b>OTHER REFERENCES (Including Author, Title, Data, Pertinent Pages, etc.)</b>   |    |  |          |  |  |  |                               |
| <u>BT</u>  | AW | J. B. BICKING, et al., J. Med. Chem., vol. 8, no. 5, pp. 638-642, "PYRAZINE DIURETICS. I. N-AMIDINO-3-6-HALOPYRAZINECARBOXAMIDES", 1965.   |          |  |  |  |                               |
| <u>BT</u>  | AX | R. F. EPAND, et al., British Journal of Cancer, vol. 63, no. 2, pp. 247-251, "REVERSAL OF INTRINSIC MULTIDRUG RESISTANCE IN CHINESE HAMSTER OVARY CELLS BY AMILORIDE ANALOGS", 1991. |          |  |  |  |                               |
| <u>BT</u>  | AY | T. M. COCKS, et al., British Journal of Pharmacology, vol. 95, no. 1, pp. 67-76, 1988.   |          |  |  |  |                               |
| <u>BT</u>  | AZ | T. R. KLEYMAN, et al., American Journal of Physiology, vol. 260, no. 2, Pt. 1, pp. C271-C276, 1991.  |          |  |  |  |                               |
| Examiner <u></u>  |    |  |          |  | Date Considered <u>19 OCTOBER 2006</u> |  |                               |
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| <b>FOREIGN PATENT DOCUMENTS</b>  |    |   |      |  |  |                                 |                               |
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| <b>OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)</b>   |    |   |      |  |  |                                 |                               |
| <b>ZT</b>  | AW | K. E. BARRETT, et al., Annual Rev. Physiol. vol. 2000, no. 62, pp. 535-572.   |      |  |  |                                 |                               |
| <b>ZT</b>  | AX | R.F. Epand, et al., "REVERSAL OF INTRINSIC MULTIDRUG RESISTANCE IN CHINESE HAMSTER OVARY CELLS BY AMILORIDE ANALOGS", Br. J. Cancer (1991), 63, pp. 247-251.  |      |  |  |                                 |                               |
| <b>ZT</b>  |    | Kim E. Barrett, et al., "CHLORIDE SECRETION BY THE INTESTINAL EPITHELIUM: MOLECULAR BASIS AND REGULATORY ASPECTS", Annu. Rev. Physiol. 2000, 62, pp. 535-572. |      |  |  |                                 |                               |
| <b>ZT</b>  | AZ | Copy of Form PCT/IPEA/408, Written Opinion for International Application No. PCT/US03/04817, filed February 19, 2003.   |      |  |  |                                 |                               |
| Examiner    |    |   |      |  | Date Considered <b>19 OCTOBER 2006</b> |                                 |                               |
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